

the group consisting of circulating microparticles, stimulated procoagulant cells and both circulating microparticles and stimulated procoagulant cells, comprising:

- (a) mixing a sample containing said member with a purified receptor which is specific for a phospholipid, under conditions to form a complex of the purified receptor and said member, wherein said purified receptor is bound directly or indirectly to a solid phase,
- (b) removing unbound components, and
- (c) determining said complex bound to said solid phase.

37. The method according to claim 36, wherein said complex is determined directly on said solid phase.

38. The method according to claim 36, wherein said complex is determined after removing said complex from said solid phase.

39. The method according to claim 36, wherein said purified receptor is annexin V.

40. The method according to claim 39, further comprising adding calcium ions in step (a).

41. The method according to claim 36, wherein said purified receptor is bound to the solid phase via a specific binding pair comprising a first and a second binding pair

member, and wherein said first binding pair member is attached to the solid phase and said second binding pair member is coupled to said purified receptor.

42. The method according to claim 36, wherein in step (c) the complex is determined by detecting any activation of prothrombin (factor II) to thrombin (factor IIa).

43. The method according to claim 42, wherein inhibitors of thrombin, Factor Xa or both thrombin and Factor Xa are present during step (a).

44. The method according to claim 42, wherein the activation of prothrombin to thrombin is detected by reacting the complex with a reagent comprising factor V, factor Xa, prothrombin (factor II) and calcium-ions, stopping the reaction by complexation of the calcium-ions, and determining thrombin by its ability to hydrolyze a chromogenic substrate.

45. A method for determining a special category or subgroup of a member selected from the group consisting of circulating microparticles, stimulated procoagulant cells and both circulating microparticles and procoagulant cells, comprising:

- (a) mixing a sample containing said member with a receptor I specific for a phospholipid, wherein said receptor is bound directly or indirectly to a solid phase, under conditions to form a complex of solid phase bound receptor I and said member,
- (b) binding a receptor 2 to said member wherein receptor 2 is specific for a marker of the special category or subgroup of circulating

microparticles and stimulated procoagulant cells to be determined,

- (c) removing unbound components from said solid phase prior to step (d)
- (d) determining any complex of receptor 1; said member; and receptor 2.

46. The method according to claim 45, wherein steps (a) and (b) are conducted simultaneously.

47. The method according to claim 45, wherein said receptor 2 is an antibody specific for a marker of the special category or subgroup wherein said special category or subgroup is selected from the group consisting of thrombocytes, endothelial cells and monocytes.

48. The method according to claim 47, wherein said marker for thrombocytes is selected from the group consisting of GPIb, GPIX, GPIIb/IIIa, and thrombospondin.

49. The method according to claim 47, wherein said marker for endothelial cells is thrombodulin.

50. The method according to claim 47, where said marker for monocytes is CD14.

51. The method of claim 50, wherein in step (b) the binding is determined by

detecting any activation of prothrombin (factor II) to thrombin (factor IIa).

✓ 52. A method for screening for the presence of phospholipid-binding antibodies in a blood sample comprising the steps of :

- (a) obtaining a blood sample from a patient suspected of having an increased thrombotic risk;
- (b) mixing said blood sample with a member selected from the group consisting of microparticles, stimulated procoagulant cells, both microparticles and stimulated procoagulant cells, and synthetic phospholipid-containing liposomes under conditions which allow binding of any phospholipid-binding antibodies present in said blood sample to said member, wherein said member is bound to a solid phase, and
- (c) determining any binding of any phospholipid-binding antibodies to said member.

53. The method according to claim 52, wherein in step (c) the antibodies are determined by measuring any precipitation of said member.

54. The method according to claim 52, wherein in step (c), the antibodies are determined using specific labeled receptors to the phospholipid binding antibodies, wherein said specific labeled receptors are selected from the group consisting of anti-Fc antibodies, anti-human immunoglobulin antibodies, anti-human-IgA antibodies, anti-human-IgG antibodies, anti-human-IgM antibodies, anti-light chain antibodies, protein A and protein G.

55. The method according to claim 54, wherein said member is biotinylated and bound to a streptavidin- or avidin-coated solid phase.

56. The method according to claim 55, wherein said member is biotinylated by inserting biotinylated phosphatidylethanolamine or biotinylated phosphatidylcholine into said microparticles and/or stimulated procoagulant cells prior to mixing said member with said blood sample.

57. The method according to claim 55, wherein said member is a synthetic phospholipid-containing liposome which is biotinylated by producing said liposomes in the presence of biotinylated phosphatidylethanolamine and/or biotinylated phosphatidylcholine.

58. The method according to claim 54 wherein said member is bound to an annexin-V-coated solid phase.

59. The method according to claim 52, wherein said member contains additional proteins on its outer surface.

60. The method according to claim 59, wherein said additional proteins are selected from the group consisting of  $\beta$ 2-glycoprotein 1, prothrombin, protein S and protein C.

61. A method for screening for diseases associated with cell damage or cell death by determining circulating apoptotic bodies, comprising the steps of:

- (a) mixing a sample suspected of containing circulating apoptotic bodies with a receptor directed to a subgroup-specific compound exposed on said circulating apoptotic bodies, [and]
- (b) determining any binding of said circulating apoptotic bodies, to said receptor, and
- (c) correlating the binding of said circulating apoptotic bodies to the presence of the disease.

62. The method according to claim 61, wherein said receptor is directed to phosphatidylserine on the surface of said apoptotic bodies.

63. The method according to claim 61, wherein said disease is selected from the group consisting of AIDS, cancer and paroxysmal nocturnal hemoglobinuria--

REMARKS

The above amendment to the claims has been made to correct the multiple dependency of the claims and to put the application in better condition for examination.

In the event that any fees are due in connection with this paper, please charge our Deposit Account No. 01-2300.

Respectfully submitted,

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